

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

ATTY.'S DOCKET: EILAT=3

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| In re Application of: |) | Confirmation No.: 7541 |
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| Eran EILAT |) | Art Unit: 1616 |
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| Appln. No.: 10/582,712 |) | Examiner: Mina Haghighatian |
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| For: COMPOSITIONS FOR TREATMENT) |) | |
| OF EAR DISORDERS... |) | |

DECLARATION OF RODRIGO YELIN

Honorable Commissioner for Patents
U.S. Patent and Trademark Office
Randolph Building, Mail Stop Amendments
401 Dulany Street
Alexandria, VA 22314

I, the undersigned Rodrigo Yelin, Ph.D., hereby
declare and state as follows.

I hold a Ph.D. in Biochemistry from the Hebrew
University of Jerusalem, M.Sc. in. Physiology from the Hebrew
University of Jerusalem, and a B.Sc. in Biology from the
Hebrew University of Jerusalem.

I am presently the COO and Head of Research and
Development of OTIC PHARMA, Ltd., Israel (hereinafter OTIC).
Prior to this I was Director of Computational Genomics and
Project Manager at EVOGENE Ltd., Israel, and before that I
served as Project Leader at COMPUGEN Ltd., Israel. I have

published scientific articles in highly regarded journals. A true and correct copy of my Curriculum Vitae is attached hereto as Exhibit A.

OTIC has sponsored certain clinical trials that are described below as Studies #1 and #2. I was the Study Director of these trials. As such I either created or critically reviewed the protocols used and I reviewed all of the reports from the twelve doctors at two different clinical centers that conducted the tests. Accordingly, I have direct knowledge of the steps that were taken and the results of those steps.

Submitted herewith is the publication of Marom et al. "Comparison of safety and efficacy of foam-based versus solution-based ciprofloxacin for acute otitis externa" *Otolaryngology-Head and Neck Surgery*, 143:492-499 (2010). This paper describes the protocol and the results of a clinical trial sponsored by OTIC, which I will refer to as Study #1.

As the Study Director in charge of this study, I can state of my own personal knowledge that the protocol recited in the Marom paper and the results disclosed therein are true and correct.


Following the results of Study #1, a second clinical trial took place which I will refer to hereinafter as Study

#2. Attached hereto as Exhibit B, are the protocol and results of Study #2.

As the Study Director in charge of Study #2, I can state of my personal knowledge that the protocol and results set forth in Exhibit B are true and correct.

I hereby further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

22 February 2011
Date



Rodrigo Yelin

Rodrigo Yelin, PhD

Date of Birth: 06 October, 1971, Argentina
Date of Aliyah: 09 March, 1989
Nationality: Israel, Argentina

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Professional Experience



2008 – Present **Otic Pharma Ltd.**, Or-Yehuda, Israel

General Manager and Head of R&D

- Managed all the company aspects, including R&D, legal, financial and Intellectual property
- Led the development of the company first product: from writing specifications to the successful completion of Phase II studies.
- Managed the development, testing and pre-clinical animal studies and safety and efficacy studies in humans using in-house employees and service providers.
- Managed the planning and execution of a Phase II Clinical Trial in Israel which included the preparation of the study protocol, the identification of sites, obtaining the approval from ethics committees, allocating CROs for study monitoring and data management and medical writing services. I also served as Study Director.
- Prepared all R&D reports for the Chief Scientist, for Business needs, for Board of Directors.
- Raised the initial funds for the company creation.

2004 – 2008

Evogene Ltd. - Rehovot, Israel

In addition to the positions detailed below I routinely presented the company in business-related meetings and scientific conferences.



Project Manager NUE, Nitrogen Use Efficiency in plants *

** The project was licensed in 2008 to Monsanto Co.*

Managed all the aspects related to the project: from strategy definition to planning and execution, intellectual property and final commercialization:

- Prepared research and management plans, Gantt's and budget estimations.
- Supervised the timely completion of the project tasks managing a team of 15 employees from various units: bioinformaticians, molecular and tissue culture scientists, plant growers.
- Established novel technologies: high-throughput screening assays and a digital imaging system devised for the automatic-analysis of thousands of transgenic plants.

Director of Computational Genomics

- Linked all the company's databases (internal and external) to facilitate the execution of multidimensional queries and implemented straightforward visualization tools.
- Managed the creation of the company's gene discovery platform ("*Athlete*") that allows for advanced cross-species comparative genomics-based queries.

1999 – 2004 **Compugen Ltd.** - Tel Aviv, Israel



Leader of Cancer Marker Discovery Project

- Organized a cancer expression database and designed a series of bioinformatic queries aimed for the discovery of potential markers for the Diagnostics field.
- Assembled the company's cancer tissue bank seeking for providers worldwide.
- Established the wet-lab methodology used to validate the potential marker candidates.

Research Scientist, Team Leader of Cloning Group

- Conducted and supervised several cloning projects for internal and external customers.
- Expedited the group productivity introducing high operational standards.
- Initiated a written reporting and briefing routine which included clear action items that was later adopted by all the lab groups.

1999 – 2000 **Institute for Vaccine Testing and Development, Army Health Division,
Medical Corps, IDF** - Tel Hashomer, Israel



Staff Scientist (as part of the military service in the Israeli Defense Forces)

- Participated in the development of dental caries-vaccines using modified enteropathogenic bacteria.
- Implemented the use of Pulse Field Gel Electrophoresis (PFGE) for strain identification.

1994 – 1999 **Hebrew University of Jerusalem** - Jerusalem, Israel

Laboratory Instructor, Teacher Assistant

- Trained, managed and coached graduated and undergraduate students in the lab work
- Teacher Assistant in the Genetics and Physiology Departments

Education

1997 - 1999 **Doctorate, Hebrew University of Jerusalem, Israel (HUJI)**

PhD Thesis devoted to "Pharmacological and Molecular Dissection of the Vesicular Monoamine Transporter (VMAT)", supervised by Prof. Shimon Schuldiner

1994 - 1996 **Master in Sciences (M.Sc.), Hebrew University of Jerusalem**
From the Physiology Dept. given as part of the PhD program

1992 - 1994 **Biology (B.Sc.), Hebrew University of Jerusalem**
Honoured Cum Laude

Military Service

1999-2000 Army Health Division, Medical Corps Headquarters - Tel Hashomer.

Honours and Awards

1995 Polak Foundation Prize for Outstanding Research Performed by a Young Investigator

Languages

Hebrew, English, Spanish.

Interests and Hobbies

Scuba Diving. Backpacking travel. Trekking.

Patent Applications

1. Yelin R. Khosravi, R, Savitzky K. (2002), Sequences of trail variants, United States Patent and Trademark Office, Application Number: 20020061525
2. Levanon EY, Eisenberg E, Yelin R. Nemzer S, Shemesh R, (2005), Systematic Mapping of Adenosine to Inosine editing sites in the Human Genome. (WO/2005/087949)
3. Ronen G, Gold E, Yelin R. Meissner R, Karchi H, Ayal S (2005) Polynucleotides and Polypeptides Involved in Plant Fiber Development and Methods of Using Same. (WO/2005/121364)
4. Karchi H, Ronen G, Yelin R. Rabinovich L. (2006) Methods of Increasing Abiotic Stress Tolerance and/or Biomass in Plants and Plants Generated Thereby. (WO/2007/020638)
5. Yelin R. Shoshan A, Gold E, Ayal S, Karchi H (2006) Isolated Polypeptides, Polynucleotides Encoding Same, Transgenic Plants Expressing Same and Methods of Using Same. (WO/2007/049275)
6. Cabiri O, Yelin R. Zlatkis E, Eilat E. (2008) Multiple-metered dispenser (WO/2010/076786)
7. Yelin R. and Eilat E. (2008) Otic Foam formulations (WO/2010/143186)

Publications

1. Schuldiner S, Steiner-Mordoch S, Yelin R. Wall SC, Rudnick G. "Amphetamine derivatives interact with both plasma membrane and secretory vesicle biogenic amine transporters". Mol Pharmacol. 1993 Dec;44(6):1227-31.
2. Schuldiner S, Shirvan A, Stern-Bach Y, Steiner-Mordoch S, Yelin R. Laskar O. "From bacterial antibiotic resistance to neurotransmitter uptake. A common theme of cell survival". Ann N Y Acad Sci. 1994 Sep 15;733:174-84.

3. Yelin R, Schuldiner S. "The pharmacological profile of the vesicular monoamine transporter resembles that of multidrug transporters". FEBS Lett. 1995 Dec 18;377(2):201-7.
4. Schuldiner S, Steiner-Mordoch S, Yelin R. "Molecular and biochemical studies of rat vesicular monoamine transporter". Adv Pharmacol. 1998;42:223-7.
5. Yelin R, Schuldiner S. "Purification of vesicular monoamine transporters: from classical techniques to histidine tags". Methods Enzymol. 1998;296:64-72.
6. Yelin R, Steiner-Mordoch S, Aroeti B, Schuldiner S. "Glycosylation of a vesicular monoamine transporter: a mutation in a conserved proline residue affects the activity, glycosylation, and localization of the transporter". J Neurochem. 1998 Dec;71(6):2518-27.
7. Yelin R, Rotem D, Schuldiner S. "EmrE, a small Escherichia coli multidrug transporter, protects Saccharomyces cerevisiae from toxins by sequestration in the vacuole". J Bacteriol. 1999 Feb;181(3):949-56.
8. Yelin R, Schuldiner S. "Vesicular monoamine transporters heterologously expressed in the yeast Saccharomyces cerevisiae display high-affinity tetrabenazine binding". Biochim Biophys Acta. 2001 Feb 9;1510(1-2):426-41.
9. Eisenberg I, Hochner H, Levi T, Yelin R, Kahan T, Mitran-Rosenbaum S. "Cloning and characterization of a novel human gene RNF38 encoding a conserved putative protein with a RING finger domain". Biochem Biophys Res Commun. 2002 Jun 28;294(5):1169-76.
10. Yelin R, Schuldiner S. "Vesicular Neurotransmitter Transporters: Pharmacology, Biochemistry and Molecular Analysis. Neurotransmitter Transporters" (ed. M. Reith) 2002 Humana Press, Totowa, NJ:313-354.
11. Yelin R, Dahary D, Sorek R, Levanon EY, Goldstein O, Shoshan A, Diber A, Biton S, Tamir Y, Khosravi R, Nemzer S, Pinner E, Walach S, Bernstein J, Savitsky K, Rotman G. "Widespread occurrence of antisense transcription in the human genome". Nat Biotechnol. 2003 Apr;21(4):379-86.
12. Levanon EY, Eisenberg E, Yelin R, Nemzer S, Hallegger M, Shemesh R, Figelman ZY, Shoshan A, Pollock SR, Sztybel D, Olshansky M, Rechavi G, Jantsch MF. "Systematic identification of abundant A-to-I editing sites in the human transcriptome". Nat Biotechnol. 2004 Aug;22(8):1001-1005.
13. Marom T, Yelin R, Goldfarb A, Rakover Y, Shlizerman L, Eilat E, Roth Y. " Comparison of safety and efficacy of foam-based versus solution-based ciprofloxacin for acute otitis externa". Otolaryngol Head Neck Surg. 2010 Oct;143(4):492-9.

Study #2: Clinical Superiority

The objective of the study was to assess whether a single daily application of the foam formulation provides equivalent therapeutic effect in the treatment of acute diffuse Otitis Externa as the approved dose of Ciloxan ear drops (applied twice a day). Besides the difference of the dosing regimen the study was essentially similar as the study detailed above. The per-protocol analysis included 14 patients, 8 patients were randomized to the "once-a-day" treatment of the Foam formulation and 6 patients were randomized to the twice daily treatment of Ciloxan ear drops. Both treatments lasted for 7 days. The results shown in Table 1 below show that the 8 patients treated with a single daily application of the Foam formulation were considered cured upon completion of the treatment, demonstrating that only 7 doses of Foam formulation are sufficient to cure Otitis externa, while 14 doses are required when using ear drops containing the same antibiotic, at the same level. The Foam formulation presents, therefore, a major advantage to the user in terms of efficacy and safety as it requires only half of the amount of antibiotic to obtain the desired therapeutic effect while reducing two-fold the potential side effects of the antibiotic.

Table 1: Summary of the clinical results - Study 2

| Clinical Response | Ciprofloxacin Foam Formulation Once-a-day use for 7 days (n=8) | Ciloxan Ear Drops Twice Daily for 7 days (n=6) |
|-------------------|--|---|
| Resolution | 87.5 % (7 out of 8) | 83.3 % (5 out of 6) |
| Improvement | 12.5 % (1 out of 8) | 16.7 % (1 out of 6) |
| Failure | 0% (0 out of 6) | 0% (0 out of 6) |